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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/571,469	03/13/2006	Frank Mattner	286808US0PCT	6417

22850 7590 12/07/2009

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EXAMINER	
KOLKER, DANIEL E	
ART UNIT	**PAPER NUMBER**
1649	

NOTIFICATION DATE	DELIVERY MODE
12/07/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/571,469	MATTNER ET AL.	
	Examiner	Art Unit	
	DANIEL KOLKER	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/24/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks and amendments filed 17 November 2009 have been entered. Claims 5-11 are pending and under examination.

Withdrawal of Finality

2. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn. The examiner concedes that the previous office action insufficiently explained the rejection under 35 USC 103(a).

Withdrawn Rejections and Objections

3. The following rejections and objections set forth in the previous office action are withdrawn:

A. The objections to the claims are withdrawn in light of the amendments which correct the minor informalities.

B. The rejections under 35 USC 103(a) are withdrawn in light of the arguments. New rejections follow.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 5-8 and 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over DeMattos 2001 (Proc Natl Acad Sci USA 98:8850-8855) in view of Kojima 2001 (J. Biochem. Biophys. Methods 49:241-251).

The teachings of DeMattos have been set forth previously. Briefly, the reference teaches that peripheral administration of a monoclonal antibody against Aβ, called m266, leads to a 1000-fold increase in the amount of Aβ in the bloodstream and a decrease in the amount of this toxic protein in the brains of mice. DeMattos hypothesizes that peripherally administering the antibody alters the equilibrium of Aβ between brain and plasma, suggesting that after circulating Aβ is sequestered by the blood, more Aβ exits the brain. That is, by binding to and sequestering Aβ in the periphery, less Aβ is freely circulating. This changes the balance of Aβ between the blood and the brain, and in order to compensate for the decreased Aβ in the blood, Aβ exits the brain and enters the bloodstream, explaining the large increase in circulating Aβ observed (see p. 8851 first column last complete paragraph, and p. 8853 last complete paragraph). The m266 antibody used binds to an epitope within residues 13-28 of Aβ (DeMattos, p. 8851, first paragraph of the Results and Discussion section), so it will bind to both Aβ40 and Aβ42, as recited in claims 6 - 8. The PDAPP mice can be construed as both suffering from AD as recited in claim 10 and at risk of AD as recited in claim 11. DeMattos suggests that antibodies against Aβ can be used to drawn Aβ out of the brain and clear it from the patient, which would be therapeutic in patients with AD; see p. 8854 last paragraph. However while DeMattos suggests using antibodies against Aβ to remove this protein from the brain and into the blood, the reference does not explicitly teach contacting the blood or plasma flow of a patient with an apheresis device that has the anti-Aβ antibodies attached to the surface of a solid carrier as recited in claim 5, rather the teachings of DeMattos are only on point to administering the antibody to animals with or at risk of disease.

Kojima teaches treatment of amyloid diseases by extracorporeal apheresis of plasma over an immunoaffinity membrane. Specifically, Kojima teaches that antibodies against either β2-macroglobulin or serum amyloid P can be immobilized on a membrane, and that when the plasma from a subject is passed through an apheresis device containing such a membrane, a large percentage of the relevant protein is removed from the serum. See for example abstract, as well as p. 243 for description of how to prepare the antibody-immobilized gel column. See p. 244 final paragraph for teaching that high levels of β2-macroglobulin are deleterious to health

and lead to amyloidosis, and p. 245 first complete paragraph for teaching that over 90% of circulating β2-macroglobulin was trapped by the column with the antibody against β2-MG on it. Additionally at p. 247 first complete paragraph Kojima teaches anti-SAP antibody can remove over 90% of this protein from plasma. The reference therefore teaches one of ordinary skill in the art how to prepare an apheresis apparatus comprising antibodies against amyloid-inducing polypeptides immobilized on a solid surface, and teaches one of ordinary skill how to use such an apparatus to remove these amyloid-causing proteins from the bloodstream of a patient susceptible to disease. However Kojima does not teach methods of treating Alzheimer's disease or using antibodies against Aβ.

Nevertheless, it would have been obvious to one of ordinary skill in the art to modify the teachings of DeMattos, by using an antibody-based apheresis system as taught by Kojima, thereby arriving at the invention encompassed by claims 5-8 and 10-11. Doing so would have been obvious, since DeMattos teaches that contacting blood with antibodies against Aβ is therapeutic for Alzheimer's disease, and that the antibodies need not reach the brain to have their effect (see for example DeMattos, p. 8850 paragraph spanning the two columns and p. 8854 second column first complete paragraph). Note that the in vitro data on p. 8850 provide evidence that support the hypothesis of the antibody acting as a sink and altering the equilibrium of the system. Of course one way to sequester circulating Aβ in the periphery is to administer an antibody as taught by DeMattos, but an artisan of ordinary skill would immediately understand that the methods of Kojima would also effectively remove circulating Aβ from the patients, if only they were modified to use an anti-Aβ antibody rather than an anti-β2MG or anti-SAP antibody. It would be reasonable to expect success, as Kojima demonstrates that the method of using an aphersis device with antibodies is effective to remove circulating amyloid proteins, so one of ordinary skill would have reasonably expected that other amyloid proteins could be removed by the same technology.

In the remarks filed 17 November 2009, applicant argued that the method as claimed would not have been obvious over DeMattos. The examiner respectfully disagrees and notes that the newly-applied reference by Kojima provides a reasonable expectation of success as well as a motivation to use antibodies in an apheresis machine, as claimed. Applicant argues that interaction of m266 with plasma and detection of this interaction by the immune system is crucial for DeMattos's methods to work. The examiner respectfully disagrees and notes that DeMattos shows that the method works in vitro across a dialysis membrane as well. Clearly the

binding of Aβ to an antibody, even in the absence of an immune system, is sufficient to change the equilibrium of this small protein and allow for passage across a semi-permeable membrane.

5. Claims 5-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over DeMattos in view of Kojima as applied to claims 5-8 and 10-11 above, and further in view of Boos (U.S. Patent 5,679,775, issued 21 October 1997).

The reasons why claims 5 - 8 and 10 - 11 are obvious over DeMattos in view of Kojima are set forth above. While Kojima teaches a column within an apheresis device, which is suitable for removing Aβ from biological fluids, the reference does not explicitly teach a sterile pyrogen-free column as recited in claim 9.

Boos teaches sterile pyrogen-free columns for apheresis. See Example 1 spanning columns 6 - 7. The reference teaches that the columns can be used to remove disease related proteins from human blood or plasma; see column 6 lines 17 - 42. However Boos does not teach sterile pyrogen-free apheresis devices comprising antibodies that bind Aβ or APP.

It would have been obvious to one of ordinary skill in the art to use sterile pyrogen-free columns as taught by Boos in the methods rendered obvious by DeMattos in view of Kojima, thereby arriving at the invention of claim 9. The motivation to do so would be to use a device that would be less likely to infect patients, as sterile pyrogen-free materials would pose less of a risk of infection than the laboratory columns taught by Sen.

Maintained Rejections

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 5 - 11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22 – 27 of copending Application No. 11/571970. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in the '970 application are specific as they require an additional step (administration of an agent) beyond the step of apheresis as claimed herein. The instant claims are generic, as they require only the step of using the apheresis device, which also appears in independent claim 22 of the '970 application. As the claims in the '970 application are species, they would anticipate the instant claims 5 - 11. Note that at p. 11 of the specification of the '970 application, anti-Aβ antibodies are indicated to be preferred components of the apheresis device, and that sterile pyrogen-free columns are preferred.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant did not traverse the examiner's rejection for obviousness-type double-patenting, but requested withdrawal of the rejection assuming the claims were otherwise allowable. As set forth above, the claims are not allowable, so this rejection stands.

Conclusion

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANIEL KOLKER whose telephone number is (571)272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel E. Kolker/
Primary Examiner, Art Unit 1649
December 2, 2009